CLAIMS

WHAT IS CLAIMED IS:

1. An isolated nucleic acid molecule comprising a polynucleotide having a nucleotide sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a polynucleotide fragment of SEQ ID NO:1 or a polynucleotide fragment of the cDNA sequence included in ATCC Deposit No: PTA-2766, which is hybridizable to SEQ ID NO1;

(b) a polynucleotide encoding a polypeptide fragment of SEQ ID NO:2 or a polypeptide fragment encoded by the cDNA sequence included in ATCC Deposit No: PTA-2766, which is hybridizable to SEQ ID NO:1;

(c) a polynucleotide encoding a polypeptide domain of SEQ ID NO:2 or a polypeptide domain encoded by the cDNA sequence included in ATCC Deposit No: PTA-2766, which is hybridizable to SEQ ID NO:1;

(d) a polynucleotide encoding a polypeptide epitope of SEQ ID NO:2 or a polypeptide epitope encoded by the cDNA sequence included in ATCC Deposit No: PTA-2766, which is hybridizable to SEQ ID NO:1;

(e) a polynucleotide encoding a polypeptide of SEQ ID NO:2 or the cDNA sequence included in ATCC Deposit No: PTA-2766, which is hybridizable to SEQ ID NO:1, having metalloproteinase activity;

(f) a polynucleotide which is a variant of SEQ ID NO:1;

(g) a polynucleotide which is an allelic variant of SEQ ID NO:1;

(h) an isolated polynucleotide comprising nucleotides 234 to 1472 of SEQ ID NO:1, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 414 of SEQ ID NO:2 minus the start codon;

(i) an isolated polynucleotide comprising nucleotides 231 to 1472 of SEQ ID NO:1, wherein said nucleotides encode a polypeptide corresponding to amino acids 1 to 414 of SEQ ID NO:2 including the start codon;

(j) a polynucleotide which represents the complimentary sequence (antisense) of SEQ ID NO:1;

(k) an isolated polynucleotide comprising nucleotides 672 to 1472 of SEQ ID NO:1, wherein said nucleotides encode the mature polypeptide corresponding to amino acids 176 to 414 of SEQ ID NO:2; and

(l) a polynucleotide capable of hybridizing under stringent conditions to any one of the polynucleotides specified in (a)-(k), wherein said polynucleotide does not hybridize under stringent conditions to a nucleic acid molecule having a nucleotide sequence of only A residues or of only T residues.

2. The isolated nucleic acid molecule of claim 1, wherein the polynucleotide fragment comprises a nucleotide sequence encoding a human metalloproteinase protein.

3. A recombinant vector comprising the isolated nucleic acid molecule of claim 1.

4. A recombinant host cell comprising the vector sequence of claim 3.

5. An isolated polypeptide comprising an amino acid sequence at least 95% identical to a sequence selected from the group consisting of:

(a) a polypeptide fragment of SEQ ID NO:2 or the encoded sequence included in ATCC Deposit No: PTA-2766;

(b) a polypeptide fragment of SEQ ID NO:2 or the encoded sequence included in ATCC Deposit No: PTA-2766, having metalloproteinase activity;

(c) a polypeptide domain of SEQ ID NO:2 or the encoded sequence included in ATCC Deposit No: PTA-2766;

(d) a polypeptide epitope of SEQ ID NO:2 or the encoded sequence included in ATCC Deposit No: PTA-2766;

(e) a full length protein of SEQ ID NO:2 or the encoded sequence included in ATCC Deposit No: PTA-2766;

(f) a variant of SEQ ID NO:2;

(g) an allelic variant of SEQ ID NO:2;

(h) a species homologue of SEQ ID NO:2;

(i) a polypeptide comprising amino acids 38 to 156 of SEQ ID NO:2 wherein said amino acids 38 to 156 comprise the metal binding domain of SEQ ID NO:2;

(j) a polypeptide comprising amino acids 2 to 414 of SEQ ID NO:2, wherein said amino acids 2 to 414 comprise a polypeptide of SEQ ID NO:2 minus the start methionine;

(k) a polypeptide comprising amino acids 1 to 414 of SEQ ID NO:2;

(l) a polypeptide comprising amino acids 29 to 267 of SEQ ID NO:22;wherein said amino acids 29 to 267 comprise the mature polypeptide of SEQ ID NO:22;

(m)a polypeptide comprising amino acids 2 to 267 of SEQ ID NO:22; wherein said amino acids 2 to 267 comprise a polypeptide of SEQ ID NO:2 minus the start methionine;

(n) a polypeptide comprising amino acids 1 to 267 of SEQ ID NO:22 wherein said amino acids 1 to 267 comprise a polypeptide of SEQ ID NO:2 with the start methionine; and

(o) a polypeptide encoded by the cDNA contained in ATCC Deposit No. PTA-2766.

6. The isolated polypeptide of claim 5, wherein the full length protein comprises sequential amino acid deletions from either the C-terminus or the N-terminus.

7. An isolated antibody that binds specifically to the isolated polypeptide of claim 5.

8. A recombinant host cell that expresses the isolated polypeptide of claim 5.

9. A method of making an isolated polypeptide comprising:

(a) culturing the recombinant host cell of claim 8 under conditions such that said polypeptide is expressed; and

(b) recovering said polypeptide.

10. The polypeptide produced by claim 9.

11. A method for preventing, treating, or ameliorating a medical condition, comprising the step of administering to a mammalian subject a therapeutically effective amount of the polypeptide of claim 5 or the polynucleotide of claim 1.

12. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or absence of a mutation in the polynucleotide of claim 1; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or absence of said mutation.

13. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or amount of expression of the polypeptide of claim 5 in a biological sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

14. A process for making polynucleotide sequences encoding a gene product having altered metalloproteinase activity comprising,

a) shuffling a nucleotide sequence of claim 1,

b) expressing the resulting shuffled nucleotide sequences and,

c) selecting for altered metalloproteinase activity as compared to the metalloproteinase activity of the gene product of said unmodified nucleotide sequence.

15. A shuffled polynucleotide sequence produced from the process of claim 14.

16. An isolated nucleic acid molecule consisting of a polynucleotide having a nucleotide sequence selected from the group consisting of:

(a) a polynucleotide encoding a polypeptide of SEQ ID NO:2;

(b) an isolated polynucleotide consisting of nucleotides 234 to 1472 of SEQ ID NO:1, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 414 of SEQ ID NO:2 minus the start codon;

(c) an isolated polynucleotide consisting of nucleotides 231 to 1472 of SEQ ID NO:1, wherein said nucleotides encode a polypeptide corresponding to amino acids 2 to 414 of SEQ ID NO:2 including the start codon;

(d) a polynucleotide encoding the MP-1 polypeptide encoded by the cDNA clone contained in ATCC Deposit No. PTA-2766; and

(e) a polynucleotide which represents the complimentary sequence (antisense) of SEQ ID NO:41.

17. The isolated nucleic acid molecule of claim 16, wherein the polynucleotide comprises a nucleotide sequence encoding a human metalloproteinase protein.

18. A recombinant vector comprising the isolated nucleic acid molecule of claim 16.

19. A recombinant host cell comprising the recombinant vector of claim 18.

20. An isolated polypeptide consisting of an amino acid sequence selected from the group consisting of:

(a) a polypeptide fragment of SEQ ID NO:2 having metalloproteinase activity;

(b) a polypeptide domain of SEQ ID NO:2 having metalloproteinase activity;

(c) a full length protein of SEQ ID NO:2;

(d) a polypeptide corresponding to amino acids 2 to 414 of SEQ ID NO:2, wherein said amino acids 2 to 414 comprise a polypeptide of SEQ ID NO:2 minus the start methionine;

(e) a polypeptide corresponding to amino acids 1 to 414 of SEQ ID NO:2; and a polypeptide encoded by the cDNA contained in ATCC Deposit No. PTA-2766;

(f) a polypeptide corresponding to amino acids 38 to 156 of SEQ ID NO:2 wherein said amino acids 38 to 156 comprise the metal binding domain of SEQ ID NO:2;

(g) a polypeptide corresponding to amino acids 2 to 414 of SEQ ID NO:2, wherein said amino acids 2 to 414 comprise a polypeptide of SEQ ID NO:2 minus the start methionine;

(h) a polypeptide corresponding to amino acids 1 to 414 of SEQ ID NO:2;

(i) a polypeptide corresponding to amino acids 29 to 267 of SEQ ID NO:22;wherein said amino acids 29 to 267 comprise the mature polypeptide of SEQ ID NO:22;

(j) a polypeptide corresponding to amino acids 2 to 267 of SEQ ID NO:22; wherein said amino acids 2 to 267 comprise a polypeptide of SEQ ID NO:2 minus the start methionine; and

(k) a polypeptide corresponding to amino acids 1 to 267 of SEQ ID NO:22 wherein said amino acids 1 to 267 comprise a polypeptide of SEQ ID NO:2 with the start methionine.

21.) The method for preventing, treating, or ameliorating a medical condition of claim 11, wherein the medical condition is an immune disorder.

22.) The method for preventing, treating, or ameliorating a medical condition of claim 11, wherein the medical condition is a motor neuron disorder.

23.) The method for preventing, treating, or ameliorating a medical condition of claim 22, wherein the medical condition is the juvenile form of amyotrophic lateral sclerosis (ALS2).

24.) The method for preventing, treating, or ameliorating a medical condition of claim 22, wherein the medical condition is amyotrophic lateral sclerosis (ALS).

25.) The method for preventing, treating, or ameliorating a medical condition of claim 22, wherein the medical condition is an amyotrophic lateral sclerosis (ALS)-like condition.

26.) The method for preventing, treating, or ameliorating a medical condition of claim 11, wherein the medical condition is related to aberrant glutamate transport or metabolism.

27.) A computer for producing a three-dimensional representation of a molecule or molecular complex, wherein said molecule or molecular complex comprises the structural coordinates of MP-1 as provided in Table III,

wherein said computer comprises:

(a) A machine-readable data storage medium, comprising a data storage material encoded with machine readable data, wherein the data is defined by the set of structure coordinates of the model;

(b) a working memory for storing instructions for processing said machine-readable data;

(c) a central-processing unit coupled to said working memory and to said machine-readable data storage medium for processing said machine readable data into said three-dimensional representation; and

(d) a display coupled to said central-processing unit for displaying said three-dimensional representation.

28.) A method for identifying an MP-1 mutant with altered biological properties, function, or activity

wherein said method comprises the steps of:

(a) using a model of said polypeptide according to the structural coordinates of said model as provided in Table III to identify amino acids to mutate; and

(b) mutating said amino acids to create a mutant protein with altered biological function or properties.

29.) A method for designing or selecting compounds as potential modulators of MP-1

wherein said method comprises the steps of:

(a) identifying a structural or chemical feature of MP-1 using the structural coordinates of MP-1 as provided in Table III; and

(b) rationally designing compounds that bind to said feature.

30.) The method according to claim 29 wherein the potential MP-1 modulator is designed from a known modulator of metalloproteinase activity.

31.) The method according to claim 28 wherein the MP-1 mutant is a mutant with mutations in the metal binding domain comprised of the amino acids D48, E97, and H146 of SEQ ID NO:2 according to Table III with altered biological function or properties.

32.) The method according to claim 30 wherein the MP-1 feature is the metal binding domain defined by all or any portion of residues D48, E97, and H146, of the three-dimensional MP-1 structural model according to Table III, or using a portion thereof.